

a fusion protein wherein a proteinaceous molecule is fused to a functional form of a phage coat protein, and

a mutant form of said phage coat protein, wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and no copies of said functional form is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and at least one copy of said functional form.

2. (Amended) The chimaeric phage according to claim 1 wherein said phage coat protein comprises the g3 protein.

3. (Amended) The chimaeric phage according to claim 2 wherein said mutant form comprises a mutation in the D1 and/or the D2 region of said g3 protein.

4. (Amended) The chimaeric phage according to claim 3 wherein said mutation comprises a deletion of substantially all of said D1 and said D2 region of said g3 protein.

5. (Amended) The chimaeric phage according to claim 1 comprising a nucleic acid encoding said fusion protein.

6. (Amended) The chimaeric phage according to claim 1 wherein said chimaeric phage is derived from a M13, M13K07, VCSM13 or R408 phage.

7. (Amended) The chimaeric phage according to claim 1 wherein said proteinaceous molecule comprises a peptide, a protein, or a part, analogue or derivative of said peptide or said protein.

8. (Amended) The chimaeric phage according to claim 1 wherein said proteinaceous molecule comprises an antibody, a Fab fragment, a single chain Fv fragment, a variable region, a CDR region, or an immunoglobulin or a functional part of said Fab fragment, said single chain Fv fragment, said variable region, said CDR region or said immunoglobulin.

AI 9. (Amended) A chimaeric phage having a coat comprising a mixture of proteins, said mixture of proteins comprising:

a fusion protein wherein a proteinaceous molecule is fused to a phage coat protein, or to a fragment or derivative of said phage coat protein, and wherein said fusion protein is functional so as to render the chimaeric phage infectious, and

a mutant form of said phage coat protein wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and carrying said mutant form and no copies of said fusion protein is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and carrying in addition to said mutant form at least one copy of said fusion protein.

10. (Amended) The chimaeric phage according to claim 9 wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and carrying said mutant form and no copies of said fusion protein is non-infectious.

11. (Amended) The chimaeric phage according to claim 1 wherein said mutant form is further characterized in that a phage having a coat comprising said mutant form in the presence or absence of copies of said functional form is stable.

Sub D1 12. An infectious phage containing at least one copy of a mutant form of a phage coat protein, wherein said mutant form has lost the ability to mediate infection of a natural host by said infectious phage.

sub D1  
A2  
Sub. C1

13. (Amended) A phage collection comprising:  
the chimaeric phage according to claim 1, or  
an infectious phage containing at least one copy of a mutant form of a phage coat protein wherein  
said mutant form has lost the ability to mediate infection of a natural host by said infectious  
phage.

14. (Amended) The phage collection according to claim 13 wherein said phage collection  
comprises a phage display library.

Sub. C2

15. (Amended) A phage collection consisting essentially of:  
the chimaeric phage according to claim 1, or  
an infectious phage containing at least one copy of a mutant form of a phage coat protein wherein  
said mutant form has lost the ability to mediate infection of a natural host by said infectious  
phage.

16. A method for producing a phage particle comprising the steps of:  
providing a host cell with a first nucleic acid encoding a fusion protein, said fusion protein  
comprising a proteinaceous molecule fused to a functional form of a phage coat protein,  
providing said host cell with a second nucleic acid encoding a mutant form of said phage coat  
protein, said mutant form being characterized in that a phage comprising no wild type phage  
coat protein from which said mutant form is derived and having a coat comprising said  
mutant form and no copies of said functional form is less infectious than a phage comprising  
no wild type phage coat protein from which said mutant form is derived and having a coat  
comprising at least one copy of said functional form and wherein said host cell comprises an  
additional nucleic acid sequence encoding at least all other proteins, or functional equivalents  
thereof, that are essential for the assembly of said phage particle in said host cell, and  
culturing said host cell to allow assembly of said phage particle.

17. (Amended) The method according to claim 16 wherein expression of said fusion protein and/or said mutant form is regulatable by altering the culturing conditions of said host cell.

AB 18. (Amended) The method according to claim 16 wherein expression of said fusion protein and/or said mutant form is under the control of a regulatable promoter.

19. (Amended) The method according to claim 18 wherein said regulatable promoter comprises the AraC/BAD promoter or a functional equivalent of said AraC/BAD promoter.

20. (Amended) The method according to claim 16 wherein said additional nucleic acid sequence is provided by a helper phage to said host cell.

21. (Amended) The method according to claim 20 wherein said helper phage comprises said second nucleic acid.

22. (Amended) The method according to claim 16 wherein said fusion protein and said mutant form are encoded by separate nucleic acids, each comprising a unique selection marker.

23. (Amended) The method according to claim 22 wherein said separate nucleic acids each comprise a unique origin of replication.

24. (Amended) The method according to claim 22 wherein said separate nucleic acids each comprise codons that essentially do not permit a homologous recombination event between said separate nucleic acids.

25. (Amended) The method according to claim 16 wherein said phage particle comprises: a chimaeric phage having a coat comprising a mixture of proteins, said mixture of proteins comprising:

AB  
a fusion protein wherein a proteinaceous molecule is fused to a functional form of a phage coat protein, and

a mutant form of said phage coat protein, wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and no copies of said functional form is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and at least one copy of said functional form, or

an infectious phage containing at least one copy of a mutant form of a phage coat protein wherein said mutant form has lost the ability to mediate infection of a natural host by said infectious phage.

26. A helper phage comprising a nucleic acid encoding phage proteins or functional equivalents of said phage proteins that are essential for the assembly of said helper phage, said nucleic acid encoding phage proteins further encoding a mutant form of a phage coat protein wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and no copies of a functional form of said phage coat protein is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising at least one copy of said functional form wherein said functional form is characterized in that it renders a phage particle carrying said functional form in its coat infectious and wherein said helper phage does not comprise a nucleic acid encoding said functional form.

27. (Amended) The helper phage according to claim 26 wherein said phage coat protein is the g3 protein.

28. (Amended) The helper phage according to claim 27 wherein said mutant form comprises a mutation in the D1 and/or the D2 region of said g3 protein.

A4  
29. (Amended) The helper phage according to claim 28 wherein said mutation comprises a deletion of substantially all of said D1 and said D2 region of said g3 protein.

30. (Amended) The helper phage according to claim 26 wherein said mutant form is further characterized in that a phage having a coat comprising said mutant form in the presence or absence of a copy of said functional forms is stable.

---

31. A method for producing a helper phage comprising the steps of:  
providing a host cell with a first nucleic acid encoding a functional form of a phage coat protein,  
providing said host cell with a second nucleic acid encoding a mutant form of said phage coat protein wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and no copies of said functional form is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising at least one copy of said functional form wherein said host cell comprises an additional nucleic acid sequence encoding at least all other proteins or functional equivalents thereof that are essential for the assembly of said helper phage in said host cell, and  
culturing said host cell to allow assembly of said helper phage.

---

AS  
32. (Amended) The method according to claim 31 wherein said other proteins or functional equivalents thereof that are essential for the assembly of said helper phage in said host cell are encoded by said second nucleic acid.

33. (Amended) The method according to claim 31 wherein expression of said functional form and/or said mutant form is regulatable by altering the culturing conditions of said host cell.

34. (Amended) The method according to claim 31 wherein expression of said functional form and/or said mutant form is under the control of a regulatable promoter.

35. (Amended) The method according to claim 34 wherein said regulatable promoter comprises an AraC/BAD promoter or a functional equivalent of said AraC/BAD promoter.

A5 36. (Amended) The method according to claim 31 wherein said phage coat protein is the g3 protein.

37. (Amended) The method according to claim 36 wherein said mutant form comprises a mutation in the D1 and/or the D2 region of said g3 protein.

38. (Amended) The method according to claim 37 wherein said mutation comprises a deletion of substantially all of said D1 and said D2 region of said g3 protein.

39. (Amended) The method according to claim 31 wherein said first nucleic acid and said second nucleic acid each comprise a unique selection marker.

40. (Amended) The method according to claim 31 wherein said first nucleic acid and said second nucleic acid each comprise a unique origin of replication.

41. (Amended) The method according to claim 31 wherein said first nucleic acid and said second nucleic acid comprise codons that essentially do not permit a homologous recombination event between said first nucleic acid and said second nucleic acid.

42. (Amended) The method according to claim 33 wherein said helper phage comprises a nucleic acid encoding phage proteins or functional equivalents of said phage proteins that are essential for the assembly of said helper phage, said nucleic acid encoding phage proteins further encoding a mutant form of a phage coat protein wherein said mutant form is characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form and no copies of a functional form of said phage coat

A5  
protein is less infectious than a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising at least one copy of said functional form wherein said functional form is characterized in that it renders a phage particle carrying said functional form in its coat infectious and wherein said helper phage does not comprise a nucleic acid encoding said functional form.

43. (Amended) A method for the enrichment of a first binding pair member in a repertoire of first binding pair members selected from the group consisting of an antibody, an antibody fragment, a single chain Fv fragment, a Fab fragment, a variable region, a CDR region, an immunoglobulin or a functional part of said antibody, said antibody fragment, said single chain Fv fragment, said Fab fragment, said variable region, said CDR region, or said immunoglobulin, said first binding pair member being specific for a second binding pair member, said method comprising the steps of:

contacting the phage collection according to claim 13 with material comprising said second binding pair member under conditions allowing specific binding,  
removing non-specific binders, and  
recovering specific binders, said specific binders comprising said first binding pair member.

44. (Amended) The method according to claim 43 comprising the additional steps of:  
recovering from a phage a DNA sequence encoding said first specific binding pair member,  
subcloning said DNA sequence in a suitable expression vector,  
expressing said DNA sequence in a suitable host, and  
culturing said suitable host under conditions whereby said first specific binding pair member is produced.

45. A nucleic acid molecule comprising a sequence encoding a mutant form of a phage coat protein, said mutant form being characterized in that a phage comprising no wild type phage coat protein from which said mutant form is derived and having a coat comprising said mutant form

1900	1901	1902	1903	1904	1905	1906	1907	1908	1909	1910	1911	1912	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308</
------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	--------